JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Do Insomnia Complaints Cause Hypertension or Cardiovascular Disease?

Barbara Phillips, M.D., M.S.P.H.; David M. Mannino, M.D.

Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine
University of Kentucky College of Medicine, Lexington, KY

Objective: We prospectively investigated odds ratios (ORs) for development of hypertension or cardiovascular disease by endorsement of sleep complaints.

Methods: The Atherosclerosis Risk in Communities (ARIC) Study is a prospective, population-based study of cardiovascular disease. Our study sample was 8757 ARIC participants without hypertension and 11,863 ARIC participants without cardiovascular disease at baseline. We applied multivariate regression analysis to predict the ORs of development of hypertension or cardiovascular disease over 6 years of follow-up by endorsement of symptoms of difficulty falling asleep (DFA), waking up repeatedly (SCD), awakening tired and fatigued (NRS), or combinations of these symptoms. We controlled for age, sex, alcohol intake, income, smoking, diabetes, heart disease, menopausal status, depression, educational level, Body Mass Index, respiratory symptoms, and pulmonary function.

Results: Endorsement of all 3 sleep complaints predicted a slightly increased risk of cardiovascular disease (OR 1.5, 1.1-2.0) but not of hypertension. Endorsement of either DFA or SCA predicted slightly increased risk of hypertension (OR 1.2, 1.03-1.3)

Conclusions: The definition of insomnia affects its impact. A combination of 3 sleep complaints (DFA, SCD, NRS) predicted a slightly increased risk of cardiovascular disease but not hypertension, and a complaint of either DFA or SCD predicted increased hypertensive risk. It is not clear whether these modest and inconsistent effects are of clinical significance.

Keywords: Sleeping pills, lifestyle, nonrestorative sleep, sleep continuity, depression, women, aging, ARIC, epidemiology

Citation: Phillips B; Mannino DM. Do insomnia complaints cause hypertension or cardiovascular disease? *J Clin Sleep Med 2007*;3(5):489-494.

Insomnia is estimated to affect as many as one third of Americans. Although the prevalence of insomnia depends on how it is defined and diagnosed, it is easily the most commonly reported sleep problem.[1,2] Insomnia is more prevalent in women than in men at all ages.[1-6] Other reported risks for insomnia include aging,[4,5] medical illness,[4,5,7,8] sleep apnea,[9] depression, psychiatric illness,[3,6] and some lifestyle factors.[10, 11]

Insomnia is associated with reduced quality of life and may precede depression.[3] A recent cross-sectional analysis[12] found that insomnia was strongly associated with impaired quality of life and poor physical and mental health, but, as the authors noted, "the cross-sectional nature of the survey does not permit conclusions as to directions of cause and effect…." Indeed, insomnia has not clearly been shown to be causally associated with adverse outcomes. In fact, Kripke et al found a reduced mortality rate for those individuals complaining of sleeping difficulty after 6 years of follow-up.[13] We have previously reported that neither insomnia complaints nor the use of hypnotics was associated with increased mortality at 6.3 years of follow-up. [14]

On the other hand, both long sleep and short sleep are associated with increased morbidity and mortality in population-based studies.[13,15,16] Recent work with population-based studies has demonstrated an increased risk of cardiovascular disease with short (and long) sleep duration.[17-20] It is possible that insomnia complaints may not directly lead to death, but that they may predispose to factors that increase mortality risk.

Efforts to establish the prevalence, outcomes, and efficacy of treatment of insomnia have been hampered by the imprecision in its diagnosis. There are several characterizations of insomnia in the literature: difficulty falling asleep; difficulty staying asleep, early morning awakening, and nonrestorative sleep. The DSM-III-R[21] and DSM IV[22] classifications and the International Classification of Sleep Disorders, 2nd edition[23] include varying criteria for insomnia. The DSM IV criteria include complaints of sleep problems 3 times a week for a month but also daytime consequences. Few epidemiologic studies include information about daytime consequences or the frequency or severity of insomnia symptoms. The recently published Research Diagnostic Criteria for Insomnia Disorder include sleep complaints, nonrestorative sleep, and daytime impairment in the definition but do not have duration, severity, or frequency criteria.[24] The recent National Institutes of Health Consensus Conference on Insomnia concluded, "Insomnia may be defined as complaints of disturbed sleep in the presence of adequate opportunity and circumstance for sleep. The disturbance may consist of one or more of three features: (1)

Disclosure Statement
This is not an industry supported study. Drs. Phillips and Mannino have indicated no financial conflicts of interest.

Submitted for publication January, 2007
Accepted for publication March, 2007
Address correspondence to: Barbara Phillips, MD, MSPH, Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine, K528 Kentucky Clinic, 740 South Limestone St, University of Kentucky College of Medicine, 800 Rose St, Lexington, KY, 50636-0284; Tel: (859) 323-5419; Fax: (859) 257-2418; E-mail: bphil95@aol.com

difficulty in initiating sleep; (2) difficulty in maintaining sleep; or (3) waking up too early. A fourth characteristic, nonrestorative or poor-quality sleep, has frequently been included in the definition, although there is controversy as to whether individuals with this complaint share similar pathophysiologic mechanisms with the others."[25]

Another significant problem with studies of the impact of insomnia is that sleep complaints frequently coexist in individuals with medical and psychologic problems that could be the actual or primary cause of adverse associations of insomnia. In fact, the National Institutes of Health consensus conference noted, "Insomnia usually appears in the presence of at least one other disorder. Particularly common comorbidities are major depression, generalized anxiety, substance abuse, attention deficit/hyperactivity in children, dementia, and a variety of physical problems. The research diagnostic criteria for insomnia recently developed by the American Academy of Sleep Medicine indeed share many of the criteria of major depressive disorder. Studies to explain these overlaps require determining how often insomnia precedes the disorders with which it is associated and whether it continues to exist if the other disorders go into remission."

Thus, prospective studies that carefully control for comorbidities are needed to assess the impact of sleep complaints. The purpose of this study was to use well-established cohort data to investigate whether specific insomnia complaints, combinations of complaints, or use of hypnotics increased the risk of hypertension or cardiovascular disease.

METHODS

Participants

The ARIC study is a prospective study of the natural history and etiology of atherosclerotic disease and of cardiovascular disease event rates and is described in detail elsewhere.[26] The study cohort was as a probability sample of men and women aged 44 to 64 years from 4 US communities: Forsyth County, NC (Winston-Salem); Jackson, MS; Washington County, MD. (Hagerstown); and suburbs of Minneapolis, MN. Baseline examinations, tests, and interviews were conducted during 1987 to 1989, and participants subsequently were contacted on an annual basis. Survivors were invited to take part in 3 follow-up data collections at intervals of approximately 3 years. In this analysis, we used data from the second visit as the baseline for establishment of behavioral and sociodemographic variables and used survival at follow-up (mean, 6.3 + 1.1 years) as a dependent variable. In order to assess whether sleep complaints were a risk factor for development of hypertension or cardiovascular disease, we studied only those subjects who were free of hypertension or cardiovascular disease at baseline (ARIC visit 2). The study objectives, design, sampling scheme, and cohort examination procedures have been described.[26]

Variable Measurement and Definitions

Most measurements reported here were collected at the second ARIC examination (1990-1992). Three sleep complaints were available as part of the Masstricht questionnaire:

"Do you often have trouble falling asleep?" (difficulty falling asleep); "Do you wake up repeatedly during the night?" (sleep continuity disturbance); and "Do you ever wake up with a feeling of exhaustion and fatigue?" (nonrestorative sleep).[27]

Age was stratified into 5 categories: 45 to 49, 50 to 54, 55 to 59, 60 to 64, and 65 to 69. Race was classified, based on self-report, as black or white. Education level was categorized as less than high school, completion of high school, or more than high school. Body mass index was calculated as weight divided by height squared (kg/m^2) and divided into 4 categories: < 20, 20 to 24, 25 to 29, and > 30. We screened for depression with the Maastricht Questionnaire,[27] which was developed to assess vital exhaustion. This is a 21-item questionnaire that correlates with depression as assessed by the Hospital Anxiety and Depression Scale.[28] We defined as depressed the upper quartile of participants who gave a positive response to 4 or more of the following 13 questions: (1) Would you want to be dead at times? (2) Do you feel dejected? (3) Have you experienced a feeling of hopelessness recently? (4) Do you believe that you have come to a dead end? (5) Do you have the feeling these days that you just do not have what it takes anymore? (6) Do you feel like crying sometimes? (7) Do you lately feel more listless than before? (8) Do you feel that your body is like a battery that is losing its power? (9) Do you have the feeling that you cannot cope with everyday problems as well as you used to? (10) Do you have the feeling that you have not been accomplishing much lately? (11) Do you feel weak all over? (12) Do little things irritate you more than they used to? (13) Does it take you more time to grasp a difficult problem than it did a year ago? Using a modification of the criteria developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), subjects were classified according to their GOLD stages of chronic obstructive pulmonary disease (COPD): GOLD stage 3 or 4 ($FEV_1/FVC < 0.70$ and $FEV_1 < 50\%$ predicted), GOLD stage 2 ($FEV_1/FVC < 0.70$ and $FEV_1 \geq 50$ to < 80% predicted), GOLD Stage 1 ($FEV_1/FVC < 0.70$ and $FEV_1 \geq 80\%$), restricted ($FEV_1/FVC \geq 0.70$ and FVC < 80% predicted), GOLD stage 0 (presence of respiratory symptoms in the absence of any lung function abnormality), and no lung disease.[29] Respondents with positive responses to "Have you ever smoked cigarettes?" and "Do you now smoke cigarettes?" were classified as "ever smokers" and "current smokers," respectively. Diabetes was defined as a fasting glucose of > 126 mg/dL or a self-reported history of or treatment for diabetes.

Systolic and diastolic fifth-phase blood pressures were measured 3 times using a random zero sphygmomanometer in the right arm in seated participants. The mean of the last 2 measurements was used in analyses. Hypertension (both at the visit 2 and visit 4 assessment) was defined as a systolic blood pressure of greater than 160 mm Hg or diastolic greater than 95 or the use of antihypertensives. Cardiovascular disease (at both the visit 2 and the visit 4 assessment) was defined as physician-diagnosed fatal or nonfatal myocardial infarction, suspected or probable myocardial infarction, or other primary cardiac event.

We performed analyses using various insomnia complaints and combinations of complaints, including (1) a complaint of difficulty falling asleep or staying asleep; (2) a complaint of difficulty falling asleep AND staying asleep, plus a complaint of nonrestorative sleep; (3) a complaint of difficulty falling asleep OR staying asleep, plus a complaint of nonrestorative sleep.

Analysis

All analyses were conducted with SAS version 8.2 (SAS Institute, Cary, NC), SUDAAN version 8.0 (RTI, Research Triangle Park, NC) and SPSS version 10 (SPSS Inc, Chicago, IL, USA). Our primary outcomes of interest were development of new cardiovascular disease or hypertension, and the main predictors of interest in our analysis were sleep complaints, singly and in various combinations.

We also performed multinomial logistic regression analysis of the factors predicting incident cardiovascular disease (among people who were free of cardiovascular disease at visit 2) and incident hypertension (among people free of hypertension at visit 2) and people who were not available for follow-up in both cohorts. Models were adjusted for age, sex, education level, BMI, depression, lung function status, smoking status, and diabetes,

RESULTS

Tables 1 and 2 demonstrate the incidence of hypertension and cardiovascular disease, respectively, in those subjects who were free of the outcome of interest at baseline (visit 2). These tables also include descriptors and percentages of participants enrolled in the study who were not available for follow-up. Individuals who were not available for follow-up were different from those from whom data were collected at the 6-year follow-up.

Overall, 20% of the 8757 who were free of hypertension at baseline developed hypertension over the follow-up period. Similarly, 4.6% of the 11,863 individuals who were free of cardiovascular disease at baseline developed cardiovascular disease over the follow-up period.

With regard to incident hypertension (Table 3), those who endorsed a symptom of either difficulty falling asleep or sleep continuity disturbance had a slightly increased risk (odds ratio [OR] 1.2, confidence interval [CI] 1.03-1.3) of developing hypertension even after controlling for confounders, but no combination of sleep complaints predicted incident hypertension.

With regard to the development of cardiovascular disease (Table 4), the combination of all 3 sleep complaints (difficulty falling asleep, sleep continuity disturbance, and nonrestorative sleep) was associated with a slightly increased risk incident cardiovascular disease (OR 1.5, CI 1.1-2.0). The combination of difficulty falling asleep or sleep continuity disturbance plus nonrestorative sleep did not predict an increased likelihood of development of either hypertension or cardiovascular disease.

DISCUSSION

Perhaps the most important finding of this analysis is that the definition of insomnia affects its impact. The combination of difficulty falling asleep or difficulty staying asleep plus nonrestorative sleep was not associated with increased risk of hypertension or of cardiovascular disease. However, we found a modest and inconsistent effect of sleep complaints on hypertension and cardiovascular disease; those individuals who reported all 3 sleep complaints at baseline had a slightly increased risk of cardiovascular disease (but not hypertension) at follow-up, and those who reported difficulty falling asleep or sleep continuity disturbance had a slightly increased risk of hypertension (but not cardiovascular disease) at follow-up. This inconsistency in morbidities as-

Table 1—Incidence of Hypertension in the ARIC Cohort Free of Hypertension at Second Visit (Baseline for This Study), Controlling for Age, Sex, Race, Education, Body Mass Index, Depression, Lung Function, Smoking Status and Diabetes. N=8758

	N (%)	Developing hypertension, %	Not available for follow-up, %
Age category			
45-49	1,121 (12.8)	16.0	15.7
50-54	2,627 (30.0)	17.7	15.8
55-59	2,237 (25.6)	20.7	16.1
60-65	1,836 (21.0)	25.2	18.0
66-69	936 (10.7)	26.1	20.9
Sex			
Female	4,815 (55.0)	22.1	16.0
Male	3,942 (45.0)	19.1	17.9
Race			
Black	1,447 (16.5)	29.0	22.8
White	7,310 (83.5)	19.1	15.7
Education, y			
< 12	1,538 (17.6)	22.8	26.1
12	2,918 (33.3)	21.0	16.1
> 12	4,301 (49.1)	19.8	14.0
Body mass index, kg/m²			
< 20	314 (3.6)	17.2	22.3
20-24	2,951 (33.7)	16.5	16.8
25-29	3,600 (41.1)	21.5	16.1
≥ 30	1,892 (21.6)	26.4	17.4
Depression			
Yes	2,401 (27.4)	20.8	21.9
No	6,356 (72.6)	20.7	15.0
Lung Function			
GOLD 3 or 4[a]	174 (2.0)	15.5	39.1
GOLD 2	880 (10.1)	20.5	25.7
GOLD 1	965 (11.0)	18.7	16.5
GOLD 0	1,039 (11.9)	23.6	17.6
Restricted	691 (7.9)	21.7	22.1
Normal	5,008 (57.2)	20.8	13.7
Smoking Status			
Current Smoker	2,447 (27.9)	18.4	25.2
Former Smoker	2,849 (32.5)	21.3	14.7
Never Smoker	3,461 (39.5)	21.9	12.7
Diabetes			
Yes	836 (9.6)	23.9	26.1
No	7,921 (90.4)	20.4	15.9
DFA or SCD			
Yes	3,586 (40.9)	22.0	19.5
No	5,171 (59.1)	19.8	15.0
DFA or SCD and morning sleepy			
Yes	1,726 (19.7)	21.6	19.8
No	7,031 (80.3)	20.5	16.1
DFA and SCD and morning sleepy			
Yes	758 (8.7)	21.2	20.8
No	7,999 (91.3)	20.7	16.5
Total	**8,757**	**20.7**	**16.9**

DFA refers to difficulty falling asleep; SCD, sleep continuity disturbance.

[a]GOLD stage 3 or 4 (FEV1/FVC < 0.70 and FEV1 < 50% predicted), GOLD stage 2 (FEV1/FVC< 0.70 and FEV1 ≥ 50 to < 80% predicted), GOLD Stage 1 (FEV1/FVC < 0.70 and FEV1 ≥ 80%), restricted (FEV1/FVC ≥ 0.70 and FVC < 80% predicted), GOLD stage 0 (presence of respiratory symptoms in the absence of any lung function abnormality), and no lung disease.

Table 2—Incidence of Cardiovascular Disease in the Aric Cohort Free of Cardiovascular Disease at Second Visit (Baseline for This Study), Controlling for Age, Sex, Race, Education, Body Mass Index, Depression, Lung Function, Smoking Status and Diabetes N=11,863

	N (%)	Developing cardio-vascular disease, %	Not available for follow-up, %
Age Category			
45-49	1,359 (11.5)	2.5	16.6
50-54	3,279 (27.6)	4.0	16.2
55-59	3,070 (25.9)	4.5	17.6
60-65	2,711 (22.9)	5.8	19.4
66-69	1,444 (12.2)	6.0	22.9
Sex			
Female	6,641 (56.0)	3.1	18.0
Male	5,222 (44.0)	6.5	18.3
Race			
Black	2,880 (24.3)	4.1	26.2
White	8,983 (75.7)	4.8	15.6
Education			
< 12 Years	2,426 (20.5)	6.1	27.3
12 Years	3,916 (33.0)	4.6	17.2
> 12 Years	5,521 (46.5)	4.0	14.8
Body Mass Index			
< 20	358 (3.0)	3.4	24.9
20-24	3,445 (29.0)	2.7	17.9
25-29	4,766 (40.2)	5.2	17.0
≥ 30	3,294 (27.8)	5.8	19.3
Depression			
Yes	3,370 (28.4)	5.3	22.2
No	8,493 (71.6)	4.3	16.5
Lung Function			
GOLD 3 or 4[a]	222 (1.9)	7.2	41.4
GOLD 2	1,163 (9.8)	6.8	25.4
GOLD 1	1,178 (9.9)	4.7	17.2
GOLD 0	1,369 (11.5)	6.5	19.5
Restricted	1,167 (9.8)	5.9	23.9
Normal	6,764 (57.0)	3.5	15.0
Smoking Status			
Current Smoker	3,160 (26.6)	5.9	26.3
Former Smoker	3,818 (32.2)	5.3	15.6
Never Smoker	4,885 (41.2)	3.2	14.8
Diabetes			
Yes	1,641 (13.8)	7.6	26.9
No	10,222 (86.2)	4.1	16.7
DFA or SCD			
Yes	4,941 (41.7)	4.7	20.7
No	6,922 (58.3)	4.5	16.4
DFA or SCD and AM Sleepy			
Yes	2,294 (19.3)	5.1	21.3
No	9,569 (80.7)	4.5	17.4
DFA and SCD and AM Sleepy			
Yes	996 (8.4)	6.0	22.9
No	10,867 (91.6)	4.5	17.7
Total	**11,863**	**4.6**	**18.2**

DFA refers to difficulty falling asleep; SCD, sleep continuity disturbance.
[a]GOLD stage 3 or 4 (FEV1/FVC < 0.70 and FEV1 < 50% predicted), GOLD stage 2 (FEV1/FVC< 0.70 and FEV1 ≥ 50 to < 80% predicted), GOLD Stage 1 (FEV1/FVC < 0.70 and FEV1 ≥ 80%), restricted (FEV1/FVC ≥ 0.70 and FVC < 80% predicted), GOLD stage 0 (presence of respiratory symptoms in the absence of any lung function abnormality), and no lung disease.

Table 3—Odds Ratios for Development of Hypertension

Insomnia complaint	OR (CI) Hypertension at Visit 4	OR (CI) No Participation in Visit 4
DFA or SCD		
Yes	1.2 (1.03, 1.3)	1.3 (1.1, 1.4)
No	1.0	1.0
DFA or SCD and NRS		
Yes	1.1 (0.9, 1.3)	1.1 (0.9, 1.3)
No	1.0	1.0
DFA and SCD and NRS		
Yes	1.0 (0.8, 1.2)	1.0 (0.8, 1.3)
No	1.0	1.0

Controlling for age, sex, race, education, body mass index, depression, lung function, smoking status and diabetes.
Limited to subjects free of hypertension at second visit.
DFA refers to difficulty falling asleep; SCD, sleep continuity disturbance; NRS, nonrestorative sleep; OR, odds ratio; CI, confidence intervals.

Table 4—Odds Ratios for Development of Cardiovascular Disease

Insomnia complaint	OR (CI) Cardiovascular disease at Visit 4	OR (CI) No Participation in Visit 4
DFA or SCD		
Yes	1.0 (0.8, 1.2)	1.2 (1.1, 1.3)
No	1.0	1.0
DFA or SCD and NRS		
Yes	1.2 (0.9, 1.5)	1.1 (0.98, 1.3)
No	1.0	1.0
DFA and SCD and NRS		
Yes	1.5 (1.1, 2.0)	1.2 (0.98, 1.4)
No	1.0	1.0

Controlling for age, sex, race, education, body mass index, depression, lung function, smoking status and diabetes.
Limited to subjects free of hypertension at second visit.
DFA refers to difficulty falling asleep; SCD, sleep continuity disturbance; NRS, nonrestorative sleep; OR, odds ratio; CI, confidence intervals.

sociated with insomnia complaints highlights a major difficulty in assessing the impact of insomnia; a valid reliable definition of insomnia remains elusive,[30] and its component symptoms and combinations of symptoms are associated with variable outcomes. Further, whether a given constellation of symptoms represents a variant of insomnia or a marker of a more serious condition is not clear. Even the minor risks associated with insomnia complaints that we found in this study might be due to the comorbidities rather than to the insomnia symptoms. In particular, it is possible that hypertension and cardiovascular related to insomnia complaints may be due to underlying sleep apnea, which is frequently associated with insomnia.[31] Indeed, we cannot be certain that the associations that we found were not contaminated by undiagnosed sleep-disordered breathing. However, we did control for body mass index, an indirect marker of sleep apnea risk, in our analyses.

Short sleep duration is strongly linked to morbidity and mortality,[13,15-20] whereas (as the current study indicates) the association between sleep complaints (insomnia) and adverse outcomes

is less clear. Many individuals with short sleep times do not have insomnia complaints; their reasons for short sleep may include busy lifestyles, and their primary reason for lack of sleep is lack of opportunity to sleep. Insomnia, on the other hand, is generally based on self-reported dissatisfaction with the quality of sleep and includes the inability to sleep in the presence of an adequate opportunity. For example, in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, black men reported much shorter sleep durations than did white women,[32] but (as any sleep clinician knows) sleep complaints are more common in white women than in black men.[33] Blurring the lines between insomnia and short sleep may contribute to our inability to ascertain the impact of insomnia. Short sleep duration (which may overlap with insomnia) is a different entity with a different impact than complaints about the ina.bility to sleep when the opportunity exits to do so.

By necessity, we assessed insomnia complaints in this secondary analysis using the data at hand; this study was not designed to assess the relationship between sleep complaints and cardiovascular outcomes per se. Use of instruments specifically designed to capture insomnia would have been preferable, but we believe that there is some value in secondary analyses of large datasets such as the ARIC cohort.

The current study has several strengths. First, the longitudinal nature of this study allows for prospective investigation of the likelihood that sleep complaints predict adverse cardiovascular outcomes. Another strength is the ability to apply several of the sleep complaints that make up the entity of insomnia in order to assess the impact of varying definitions of insomnia. Finally, the ARIC population includes more than 13,000 well-characterized individuals, allowing for control for multiple confounders and individual characteristics. Because depression overlaps with insomnia to a great extent,[25] it is especially important to be able to control for this variable, as we were able to do. In a prospective evaluation of the relationship of a single insomnia complaint (difficulty falling asleep) to hypertension, Japanese investigators reported a positive association; although they were able to control for many important variables, they did not control for depression.[34] A 1999 review of studies assessing the relationship between insomnia complaints and coronary heart disease found 10 studies that suggested an increased risk of development of coronary events in those with difficulty falling asleep,[35] but these older papers did not consistently include and control for the multitude of variables that are relevant to this issue.

The modest and inconsistent associations that we found between sleep complaints and incident cardiovascular disease and hypertension suggest that insomnia is not a robust contributor to adverse cardiovascular events.

ACKNOWLEDGMENTS

The authors thank the staff and participants in the Atherosclerosis Risk in Communities (ARIC) study for their important contributions. The ARIC study is conducted and supported by the National Heart Lung and Blood Institute (NHLBI) in collaboration with the ARIC Study Investigators. This Manuscript was not prepared in collaboration with investigators of the ARIC study and does not necessarily reflect the opinions or views of the ARIC study or the NHLBI.

REFERENCES

1. Sateia MJ, Doghramji K, Hauri PJ, Morin CM. Evaluation of chronic insomnia. An American Academy of Sleep Medicine review. Sleep 2000;23:243-308.
2. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97-111.
3. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989 ;262:1479-84.
4. Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res 2004;56:497-502.
5. Foley DJ, Monjan AA, Brown SL, Simonsick EM, Wallace RB, Blazer DG. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep 1995;18:425-32.
6. Buysse DJ, Reynolds CF, III, Kupfer DJ, et al. Clinical diagnoses in 216 insomnia patients using the International Classification of Sleep Disorders (ICSD), DSM-IV and ICD-10 categories: a report from the APA/NIMH DSM-IV Field Trial. Sleep 1994;17:630-7.
7. Dodge R, Cline MG, Quan SF. The natural history of insomnia and its relationship to respiratory symptoms. Arch Intern Med 1995; 155:1797-800.
8. Katz DA, McHorney CA. Clinical correlates of insomnia in patients with chronic illness. Arch Intern Med 1998;158:1099-107.
9. Krakow B, Melendrez D, Ferreira E, et al. Prevalence of insomnia symptoms in patients with sleep-disordered breathing. Chest 2001;120:1923-9.
10. Cheek RE, Shaver JL, Lentz MJ. Lifestyle practices and nocturnal sleep in midlife women with and without insomnia. Biol Res Nurs 2004;6:46-58.
11. Phillips BA, Mannino D. Correlates of sleep complaints in adults: The ARIC Study. J Clin Sleep Med 2005; 1: 277-283;
12. Steward R, Besset A, Brugha T, et al. Insomnia comorbidity and impact and hypnotic use by age group in a national survey population aged 16 to 74 years. Sleep 2006; 29:1391-7.
13. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59:131-6.
14. Phillips BA, Mannino DM. Does insomnia kill? Sleep 2005;28: 965-971.
15. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. Sleep 2004;27:440-4.
16. Amagai Y, Ishikawa S, Gotoh T, Doi Y, Kayaba K, Nakamura Y, Kajii E. Sleep duration and mortality in Japan: the Jichi Medical School Cohort Study. J Epidemiol 2004;14:124-8.
17. Gottlieb DJ, Redline S, Nieto FJ, et al. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. Sleep 2006;29:1009-14.
18. Gangwisch JE, Heymsfield SB, Boden-Albala B et al. Short sleep duration as a risk factor for hypertension. Analyses of the first National Health and Nutrition Examination Survey. Hypertension 2006;47:833-9.
19. Heslop P, Smith GD, Metcalfe C, Macleod J, Hart C. Sleep duration and mortality: The effect of short or long sleep duration on cardiovascular and all-cause mortality in working men and women. Sleep Med. 2002;3:305-14.
20. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. Arch Intern Med 2003;163:205-9.
21. Diagnostic and Statistical Manual of Mental Disorders, 3rd ed, revised. Washington: American Psychiatric Association; 1987.
22. Diagnostic and Statistical Manual of Mental Disorders, 4th ed, revised (DSM-IV-R). Washington: American Psychiatric Association; 1994.

23. International classification of sleep disorders: Diagnostic and coding manual, 2nd ed. Westchester, Illinois: American Academy of Sleep Medicine; 2005.
24. Edinger J, Bonnet MH, Bootzin RR, et al. Derivation of research diagnostic criteria for insomnia: Report of an American Academy of Sleep Medicine Work Group. Sleep 2004;27: \1567-96.
25. NIH State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults. June 13-15, 2005. Washington DC, Available at: http://consensus.nih.gov/2005/2005InsomniaSOS026html.htm. Accessed: November 20, 2006.
26. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. Am J Epidemiol 1989;129:687-702.
27. Appels A, Hoppener P, Mulder P. A questionnaire to assess premonitory symptoms of myocardial infarction. Int J Cardiol 1987;17:15-24.
28. McGowan L, Dickens C, Percival C, Douglas J, Tomenson B, Creed F. The relationship between vital exhaustion, depression and comorbid illnesses in patients following first myocardial infarction. J Psychosom Res 2004;57:183-8.
29. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001;163:1256-76.
30. Summers MO, Crisostomo MI, Stepanski EJ. Recent developments in the classification, evaluation, and treatment of insomnia. Chest 2006;130:276-86.
31. Krell SB, Kapur VK. Insomnia complaints in patients evaluated for obstructive sleep apnea. Sleep Breath 2005;9:104-10.
32. Lauderdale DS, Knutson KL, Yan L, et al. Objectively measured sleep characteristics among early-middle-aged adults. The CARDIA study. Am J Epidemiol 2006;164:5-16.
33. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the Cardiovascular Health Study. Sleep 1998;21:27-36.
34. Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. J Occup Health 2003;45:344-350.
35. Schwartz S, McDowell Anderson W, Cole SR, et al. Insomnia and heart disease: a review of epidemiologic studies. J Psychosom Res 1999; 47: 313-333.